Antigen-Specific Antibody Design and Optimization with Diffusion-Based Generative Models for Protein Structures

Abstract

Antibodies are immune system proteins that protect the host by binding to specific antigens such as viruses and bacteria. The binding between antibodies and antigens is mainly determined by the complementarity-determining regions (CDR) of the antibodies. In this work, we develop a deep generative model that jointly models sequences and structures of CDRs based on diffusion probabilistic models and equivariant neural networks. Our method is the first deep learning-based method that generates antibodies explicitly targeting specific antigen structures and is one of the earliest diffusion probabilistic models for protein structures. The model is a "Swiss Army Knife" capable of sequence-structure co-design, sequence design for given backbone structures, and antibody optimization. We conduct extensive experiments to evaluate the quality of both sequences and structures of designed antibodies. We find that our model could yield competitive results in binding affinity measured by biophysical energy functions and other protein design metrics.